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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,139	12/17/2002	Anne Eckert	ST99042USPCT	1457

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EXAMINER	
HAMA, JOANNE	

ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
08/12/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)
	10/088,139	ECKERT ET AL.
	Examiner	Art Unit
	JOANNE HAMA	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,10,12,17,18,20 and 22-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,10,12,17,18,20 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)	
1) ☒ Notice of References Cited (PTO-892)	4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) ☐ Notice of Informal Patent Application
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.	6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 10, 2011 has been entered.

In the claims filed January 10, 2011, claims 1-8, 11, 13-16, 19, 21 are cancelled. Claims 9, 12, 17, 20, 22, 24 are amended.

Claims 9, 10, 12, 17, 18, 20, 22-25, drawn to a method for detecting compounds intended for the treatment of neurodegenerative diseases, are under consideration.

Maintained Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 9, 10, 12, 17, 18, 20, 22-25 remain rejected in modified form under 35 U.S.C. 103(a) as being unpatentable over Citron et al., 1998, Neurobiology of

Diseases, 5: 107-116, previously cited, in view of St. George-Hyslop et al., US Patent 6,395,960, patented May 28, 2002, previously cited, Ishii et al., 1997, Neuroscience Letters, 228: 17-20, previously cited, Borchelt et al., 1997, Neuron, 19: 939-945, previously cited, and Xia et al., 1997, The Journal of Biological Chemistry, 272: 7977-7982, previously cited, Lombardi et al., 1999, Journal of Neuroimmunology, 97: 163-171, for reasons of record, June 18, 2009, March 11, 2010, July 1, 2010.

The rejection of June 18, 2009 is copied below for Applicant's convenience.

Citron et al. teach that Abeta42 is elevated in conditioned media of cells expressing mutant but not wild type presenilin 1 (PS1). Further, the effects of two different PS1 mutations are additive when engineered into the same PS1 molecule (Citron et al., abstract). Citron et al. teach that kidney cells were stably transfected with APP695 and a PS1 double mutant and that these cells had higher levels of Abeta42 than cells that have single mutations in PS1 (Citron et al. page 111, 2nd col., under Abeta42 Effects of the PS1 Mutations M146L and L286V Are Additive). Given this teaching, Citron et al. teach that presenilin mutations have a systemwide effect of Abeta42 production and can therefore be studied in a peripheral cell line (Citron et al., page 112, 1st col. under Discussion). Citron et al. also teach that cells that predominantly make the Abeta42 protein will be useful for localizing the subcellular sites of Abeta42 production and understanding the way in which mutant presenilin alters APP proteolysis. By additional manipulations, it would be possible to generate cell lines and transgenic animals which would produce almost exclusively Abeta42 (Citron et al. page 115, 1st col., 1st parag.).

While Citron et al. do not specifically teach that transgenic mice comprising multiple mutations in PS1 exhibit apoptosis in their peripheral cells, this would be an inherent characteristic of these transgenic mice. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the

prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). It is noted, that the art at the time of filing teaches that peripheral cells that express mutant PS1 exhibit apoptosis (St. George-Hyslop et al., col. 20, 3rd parag.).

With regard to the claims being drawn to PS1 comprising at least 3 mutations or 5 particular mutations (e.g. claims 4, 5), these are known mutations in PS1 and given that Citron et al. teach that it would be ideal to make a transgenic mouse that produces almost exclusively Abeta42, an artisan would have made mice comprising additional mutations in PS1, to arrive at mice that produce more Abeta42 than the double mutant PS1 mouse made by Citron et al. It is noted that Ishii et al. teach the H163R mutation (Ishii et al., abstract), Borchelt et al. teach the A246E mutation (Borchelt et al., abstract), and Xia et al. teach the C410Y mutation (Xia et al., abstract) and that in each of these publications, these mutations lead to an increase in Abeta42. It is noted that Abeta42 is the amyloid species found in early-onset familial Alzheimer's disease (FAD) patients.

With regard to the claims being drawn to detecting compounds intended for the treatment of neurodegenerative diseases (claims 12, 20), it is noted that animal models of disease are used in screens to identify therapeutics (e.g. see St. George-Hyslop et al., abstract).

With regard to the claims being drawn to the cells being T-lymphocytes (claims 10, 18), it is noted at the time of filing, the art know of the relationship between T-cells and apoptosis. First, as indicated above, St. George-Hyslop et al. teach that peripheral cells that express mutant PS1 exhibit apoptosis. Second, Lombardi et al. teach that populations of T-cells were lower in

Alzheimer's patients versus that of normal patients and that T cells underwent apoptosis. As such, given that the art teaches that there was a relationship between T cells, apoptosis, and mutant PS1, an artisan would have screened for agents that reduced apoptosis in T cells of PS1 mutant non-human animal models.

With regard to the claims being drawn to "allowing an apoptotic phenomenon to be detected in a renewable peripheral tissue" (e.g. claim 12), it is not entirely clear what this phrase means. However, the Examiner has interpreted this to mean that changes in apoptotic activity in peripheral tissues are detected and that an artisan would have identified compounds that treat apoptosis by identifying the compounds that reduce apoptosis.

Applicant's arguments filed January 10, 2011 have been fully considered but they are not persuasive.

Applicant indicates that claims 12 and 20 are amended and recite 5 specific mutations not taught or suggested by the applied references (Applicant's response, page 4). In response, this is not persuasive. As indicated above, the mutations M146L and L286V are taught by Citron et al., the H163R mutation is taught by Ishii et al., the A246E mutation was taught by Borchelt et al., and the C410Y mutation was taught by Xia et al.

Thus, the claims remain rejected.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama whose telephone number is 571-272-2911. The examiner can normally be reached Mondays, Wednesdays, Thursdays, and Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history

information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Joanne Hama/
Primary Examiner
Art Unit 1632